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## Computational rehabilitation of neglect

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# Computational rehabilitation of neglect: using state-space models to understand the recovery mechanisms\*

Giulia Sedda<sup>1</sup>, Marcella Ottonello<sup>2,3</sup>, Elena Fiabane<sup>2</sup>, Caterina Pistarini<sup>2</sup>, Anna Sedda<sup>4</sup> and Vittorio Sanguineti<sup>1</sup>

**Abstract**—Unilateral spatial neglect is a neuropsychological syndrome often observed in right hemisphere stroke patients. The symptoms differ from subject to subject. A few rehabilitation approaches, e.g. prism adaptation, have demonstrated some effect in reducing the symptoms, but the underlying mechanisms are still largely unclear. Recently, neural models have been proposed to qualitatively describe cortical lesions, the resulting neglect symptoms and the effects of treatment. However, these predictions are qualitative and cannot be used to compare different hypotheses or to interpret symptoms at individual subjects level. Here we propose a computational model of the trial-by-trial dynamics of training-induced recovery from neglect. Neglect is modelled in terms of an impaired internal representation of visual stimuli in the left hemispace. The model assumes that recovery is driven by the mismatch between defective representations of visual stimuli and the corresponding hand positions. The model reproduces the main observations of prism adaptation experiments. Using standard system identification techniques, we fitted the model to data from a rehabilitation trial based on a novel rehabilitation approach based on virtual reality, involving reaching movements within an adaptive environment. Our results suggest that the model can be used to interpret data from individual subjects and to formulate testable hypotheses on the mechanisms of recovery and directions for treatment.

## I. INTRODUCTION

Unilateral spatial neglect (USN) is usually described as a ‘failure to report, orient toward, or respond to stimuli in contralesional space, which cannot be attributed to primary motor or sensory dysfunction’ [1]. This heterogeneous and common syndrome is most often observed after stroke. Severe and enduring neglect is far more likely associated with right hemisphere damage – up to 2/3 of right hemisphere stroke patients have neglect symptoms acutely. Many different deficits contribute to the syndrome, in variable proportions among different subjects, presumably depending on location and extent of brain damage. An inability to direct attention to

the left hemispace is considered as one of the main symptoms. It is debatable whether neglect may result from an impaired representation of space [2], which can be in multiple frames of reference (for example, retinotopic, head centred, trunk centred) or be specific to near or far space. Other investigators have argued that neglect may also reflect a directional motor impairment, with patients experiencing difficulty in initiating or programming contralesional eye or limb movements [3].

Early attempts to treat neglect were based on ‘top-down’ approaches, relying on patients’ awareness, and aimed at deliberately modifying their behaviour, for instance by encouraging patients to direct their gaze towards the contralesional space [4]. These paradigms were somehow successful in reducing neglect within the task used for training, but failed to generalise to tasks outside of the training environment. ‘Bottom-up’ strategies aim at producing an automatic change in behaviour, or recalibration of the recruited sensorimotor mechanisms. In some cases improvements in performance induced by ‘bottom-up’ approaches have been shown to generalise to tasks that were not used in training. This is the case of caloric and vestibular stimulation, contralesional limb activation, trunk rotation, vibration or electrical stimulation of neck muscles, and prism adaptation [5].

Rossetti et al. [6] examined the effects of adaptation to a prism-induced rightward horizontal displacement of the visual field in neglect patients. Immediately after adaptation, neglect improved in all clinical tests. The improvement persisted well beyond the wash-out of the adaptation effect [7]. The mechanisms of action of prism adaptation are not yet clearly understood, but the effect does not seem to be a mere consequence of the leftward motor bias developed by the right arm during prism adaptation. Rather, prism adaptation is believed to affect higher level spatial representations [6], [7]. Strategies based on virtual reality (VR) have been developed for USN assessment and rehabilitation [8]. VR approaches may provide ecological and realistic types of interaction, involving the participation in functional activities that are otherwise unsafe to perform in real life. Current approaches generally focus on remapping of space, which is strongly connected to updating of the body schema representation and multisensory integration [9]. Recently, robots have received attention for rehabilitation of neglect [10]. Robot-assisted limb activation exercise (movements of the left limb within the left hemispace) was observed to produce benefits to neglect that were similar to those obtained with conventional treatment.

Computational models have been successfully applied to

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<sup>1</sup>Giulia Sedda and Vittorio Sanguineti are with the Department of Informatics, Bioengineering, Robotics and Systems Engineering, University of Genoa, Italy (giulia.sedda@edu.unige.it, vittorio.sanguineti@unige.it)

<sup>2</sup>Marcella Ottonello, Elena Fiabane and Caterina Pistarini are with ICS Maugeri SpA SB - Istituto Genova Nervi, Genoa, Italy (marcella.ottonello@icsmaugeri.it)

<sup>3</sup>Marcella Ottonello is also with the Department of Clinical Sciences and Translational Medicine, University of Rome Tor Vergata, Rome, Italy

<sup>4</sup>Anna Sedda is with the School of Social Sciences, Heriot-Watt University, Edinburgh, UK (a.sedda@hw.ac.uk)

the study of motor learning and adaptation [11], providing important insights with respect how brain controls movement and reacts to the environment or task variables changes. Only recently these approaches have been applied to the rehabilitation field. Recently, Casadio et al. [12] used a linear dynamical model to describe the trial-by-trial evolution of the motor performance of chronic stroke survivors who underwent a rehabilitation protocol based on a robot-assisted arm extension task. These early attempts may potentially lead to a deeper understanding of the mechanisms underlying neuromotor recovery [13], [14]. In the case of neglect, Leigh et al. [15] recently proposed a computational model which involved a realistic description of the lesions in the cortical parietal areas. Their main assumption was that prism adaptation primarily influences dorsal stream structures that mediate visual guidance of actions and is typically spared in neglect [16]. The model reproduced a few symptoms of neglect, like line bisection behaviour and the beneficial effect of prism adaptation. However, model predictions are qualitative predictions and cannot be used to explain individual behaviours.

Here we apply the dynamical systems framework to model the trial-by-trial dynamics of training-induced recovery from neglect. We describe the model and show its predictions in the context of prism adaptation. We also apply the model to the study of the recovery dynamics in the context of a newly designed training protocol, based on reaching movements within an adaptive environment enriched with distractors and audio-visual cues.

## II. MATERIALS AND METHODS

### A. Computational Model

1) *Spatial attention and neglect*: Visual spatial attention is the ability to direct attention to a specific location in space. Objects at this location will be processed faster and more accurately than events at other locations. Persons with neglect are often impaired in reporting spatial targets in the left hemisphere and driving their own hand toward that target, in a way which cannot be explained by impaired movement alone. Leigh et al. [15] assumed that visual target and hand position are encoded in the parietal cortex by a population of neurons, each with a ‘preferred’ target or hand position and a bell-shaped tuning curve. The left hemisphere only encodes contralateral (right) target positions, whereas the right hemisphere encodes for targets in both hemispheres [17]. This explains why neglect symptoms are more severe when damages are located in the right hemisphere. In our simulation we used 4800 neurons, 2400 for the right hemisphere and 2400 for the left hemisphere. Each neuron was assumed to encode a preferred location respectively in the right hemisphere (left hemisphere neurons), and in both hemisphere (right hemisphere neurons). Assuming a uniform distribution of the preferred positions of these neurons, we simulated a lesion by destroying 90% of the neurons in the right hemisphere. A consequence of the lesion would be a less reliable representation of target and/or hand positions located in the left hemisphere, as shown in Figure 1 (left).

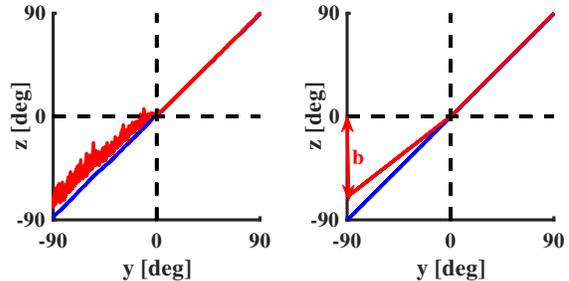


Fig. 1: Neglect is modelled as a distorted neural representation ( $z_T(t)$ ) of visual targets ( $y_T(t)$ ). Left: simulated effect of lesions in the right parietal cortex [15]. Right: proposed macroscopic model. The quantity  $b(t)$  is a measure of neglect.

In our model, we denote  $x_T(t)$  and  $x(t)$  as, respectively, target position and hand position in a person-centered coordinate frame at the end of the  $t$ -th movement trial. We also define  $y_T(t)$  and  $y(t)$  as the visually perceived target and hand position in retinotopic coordinates. We also assume that these visual stimuli are represented in the parietal cortex as  $z_T(t)$  and  $z(t)$ , respectively. We model the right-hemisphere lesion as a multiplicative term  $b(t)$ , which leads to a distorted representation of stimuli located in the left visual hemisphere:

$$z_T(t) = \begin{cases} y_T(t), & \text{if } y_T(t) \geq 0, \\ \frac{b(t)}{H} y_T(t), & \text{if } y_T(t) < 0. \end{cases} \quad (1)$$

where  $H$  denotes the boundary of the visual hemisphere. We assume the same value on both the right and the left side [18]. The targets are located within either the right ( $y_T(t) > 0$ ) or left hemisphere ( $y_T(t) < 0$ ). When  $b(t) = H$  there is no neglect, whereas  $b(t) = 0$  corresponds to the complete lack of representation of the left visual hemisphere; see Figure 1 (right). Eq. 1 reproduces, at a macroscopic level, the neural model proposed by [15]. The model predicts that neglect causes a distortion of the mapping between a visual target located in the left hemisphere and its internal representation, whose effect increases linearly with target position, as shown in Figure 1. When reaching for a visual target, hand movements are planned in terms of the internal representation of the visual target, so that:

$$x(t) = z_T(t) \quad (2)$$

Eqs. 1 and 2 predict that neglect only affects movements in the left hemisphere. In this case, there will be a mismatch between hand movements and target position,  $y_T(t)$ . The model also captures the notion that internally planned movements – like, for instance, line bisection or straight-ahead movements – are biased toward the right because the ‘center’ of the internal representation is shifted toward the right.

2) *Neglect recovery*: The mechanisms of training-induced recovery from neglect are little understood. We can only speculate that a possible driving force toward a reorganisation of the residual representation of the left hemisphere is the mismatch between visual target and hand position at the end of the movement. Such a mismatch only occurs in the left

hemisphere, which suggests that movements of the hand in the left hemisphere ( $x(t) < 0$ ) are a necessary ingredient of neglect recovery. This leaves room to a large variety of possible recovery mechanisms, and the available evidence is compatible with multiple mechanisms. As a starting point for further analysis, we tentatively assume that another condition for recovery to take place is that the visual targets are not too far left, i.e.  $y_T(t) > -b(t)$ . We hypothesise that inducing movements of the hand in areas of the workspace that are subject to neglect triggers a change in the internal representation of visually perceived targets. We make the simplifying assumption that the magnitude of adaptation is proportional to the amount of neglect, i.e.  $H - b(t)$ . The effect can be described by the following equations:

$$b(t+1) = A_n \cdot b(t) + B_n \cdot [H - b(t)] \cdot u_z(t) \quad (3)$$

The function  $u(t)$  captures the conditions which trigger a neglect improvement:

$$u_z(t) = \begin{cases} 1, & \text{if } x(t) < 0 \text{ and } y_T(t) > -b(t), \\ 0, & \text{otherwise} \end{cases} \quad (4)$$

Parameters  $0 < A_n < 1$  and  $B_n > 0$  denote, respectively, the retention rate – how much neglect at the next trial is affected by neglect at the current trial – and the recovery rate – the amount of recovery occurring when  $u_z(t) = 1$ . If the conditions are not satisfied, i.e.  $u_z(t) = 0$ , neglect will decay, i.e. will get worse.

3) *Prism Adaptation*: Wearing prisms causes a mismatch between the hand position,  $x(t)$  and its visual estimate,  $y(t)$ :

$$y(t) = x(t) + r(t) \quad (5)$$

where  $r(t)$  is the visual shift due to the prisms. A similar mismatch is caused at the level of the visual targets:

$$y_T(t) = x_T(t) + r(t) \quad (6)$$

As in Eq. 2, hand movements are planned in terms of the visual representations of the target,  $z_T(t)$ . However, similar to visuomotor rotation experiments [19] we assume that when planning a movement, subjects gradually develop an internal model  $u(t)$  of the visual perturbation. This internal model is incorporated into the motor command, so that hand position is now specified as:

$$x(t) = z_T(t) - u(t) \quad (7)$$

Exercise with prisms induces an adaptation process, aimed at developing an ‘internal model’ of the prism perturbation, i.e. the amount of correction  $u(t)$  with respect to the visual target that is necessary to minimise the error. It has been suggested [19] that the development of an internal model of the visual perturbation is driven by the mismatch between the target position and the displayed hand position. This also corresponds to the prediction error, i.e. the difference between the actual and the predicted perturbation:

$$e(t) = y(t) - y_T(t) = r(t) - u(t) \quad (8)$$

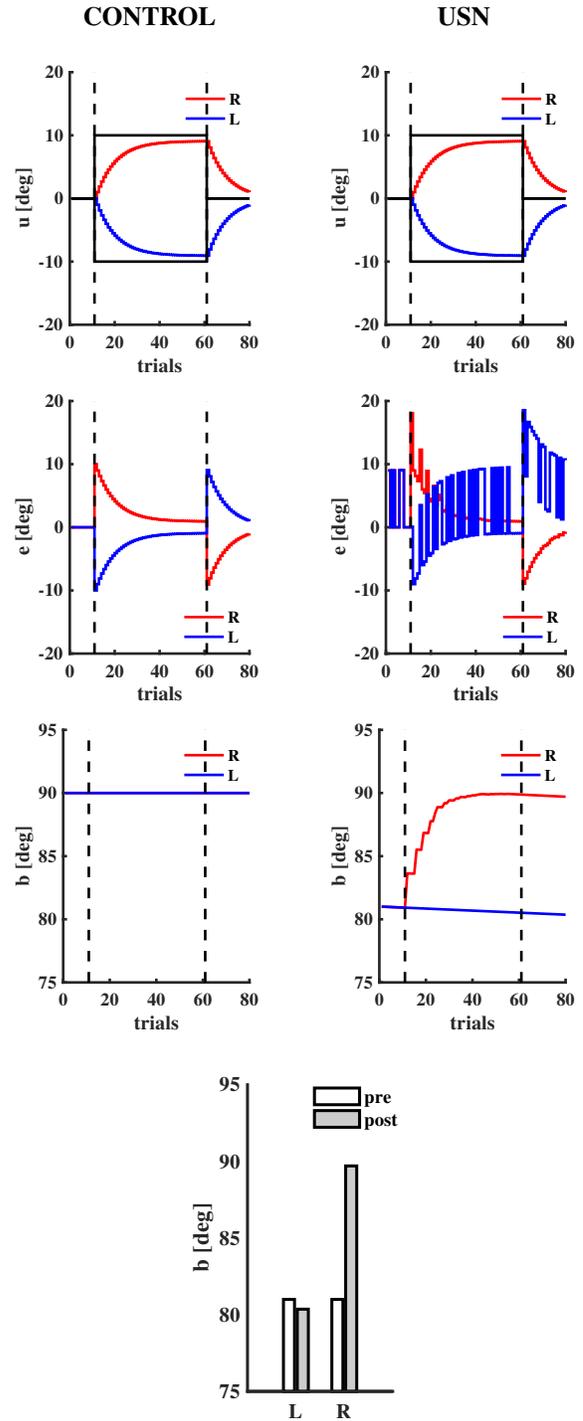


Fig. 2: Simulation results: prism adaptation in healthy (left) and neglect (right) subject. From top to bottom, the traces display the prism shifts (black) and the evolution of the internal models, the prediction errors and the measure of neglect, for both right (red) and left prism (blue). The bar plot on the bottom summarizes the change in neglect.

This error is zero if the correction term,  $u(t)$ , equals the shift  $r(t)$ . Therefore, the correction term can be interpreted as a predictor of the shift magnitude, and  $e(t)$  is a measure of the mismatch between the prism perturbation and its predictor

or ‘internal model’. However, what is available is not the visual error but rather the mismatch between the internal representations of  $y(t)$  and  $z_T(t)$ :

$$e_z(t) = y(t) - z_T(t) \quad (9)$$

If there is no neglect,  $e_z(t) = e(t)$ . We assume that prism adaptation is driven by the prediction error,  $e_z(t)$ , according to the following equation:

$$u(t+1) = A_u u(t) + B_u e_z(t) \quad (10)$$

where  $0 < A_u < 1$  and  $B_u > 0$  are, respectively, a retention rate – reflecting the build-up of the predictor from trial to trial – and a rate of adaptation – reflecting how much the predictor is modified by the observed prediction error. On the very first prism trial, there is no prediction ( $u(t) = 0$ ) and the subjects simply aim their hand at the visual target,  $z_T(t)$ . This leads to a visual error, which is exploited to correct the next prediction. From trial to trial, the prediction of the perturbation improves and the error decreases. In terms of hand movements, if  $r(t)$  is directed toward the right, from trial to trial the movements of the hand are gradually shifted toward the left. This shift triggers the recalibration mechanism described by Eqs. 3 - 4, thus resulting in a reduction of the neglect symptoms. As the latter is more persistent than the effect of prism adaptation [6], [7], we expect that the neglect retention rate,  $A_n$ , is greater than the retention rate for prism adaptation,  $A_u$ . In conclusion, training with prisms leads to a recovery from the neglect symptoms. For protocol details, see [6].

## B. Experiments

We compared the model predictions with experimental results from an ongoing rehabilitation trial, consisting of a reaching task within a virtual environment. The motivations underlying this approach are summarised in [9]. More details on the experiment can be found in [20].

1) *Experimental apparatus*: The experimental apparatus included a video projector, displaying a virtual reality environment on a 2 m × 2 m screen. Subjects sat in front of the screen, at a 2.5 m distance. A markerless motion capture sensor (Microsoft Kinect), placed below the screen, recorded the subjects’ hand movements at a 20 Hz sampling rate. The screen continuously displays the subjects’ mirror image – extracted from the depth image provided by the Kinect sensor – within a virtual scene (a tree with apples). Two speakers placed at each side of the screen provide spatialized sounds.

2) *Task and exercise protocol*: At the beginning of each trial, subjects sit in front of the screen with their hands on their knees (starting position). A target (apple) appears on the screen at random locations, evenly distributed in both hemispaces. Subjects are instructed to reach the target using their right hand as fast and accurate as possible. At the end of each movement a numeric score is provided, reflecting the movement time. If the target is not reached within a 20 s timeout, the score is considered to be zero. After each trial, subjects must return to the starting position. The virtual environment automatically adapts to subject performance

through the introduction of a variable number of distractors (rotten apples) that subjects must avoid in order to complete the trial. Targets appear one at a time, while distractors appear all together. As training proceeds, subject go through three subsequent ‘stages’, during which subjects are initially given audiovisual cues (target flashing and spatialized beep sound), then visual only, and finally no cues. The treatment protocol consisted of 30-min training sessions, five days a week, for three consecutive weeks.

3) *Subjects*: The study involved a total of four subjects with subacute right hemisphere stroke, see the Table I for demographic and clinical information, hospitalised at ICS Maugeri SpA SB - Istituto di Genova Nervi. All patients signed a consent form to participate in the study. Inclusion criteria were: unilateral neglect following a cerebro-vascular accident; dominant right hand assessed by the Edinburgh Inventory test; no previous history of psychiatric disorders or cognitive impairments (Mini-Mental State Examination); no drug or alcohol abuse. Exclusion criteria were aphasia, attention deficits and frontal syndrome, generalized hemianopia. Before the start of the treatment protocol, all subjects underwent a neuropsychological evaluation involving the following paper tests and clinical scales: Behavioural Inattention Test (BIT), Barthel Index (BI), Reading Test (RT), and Catherine Bergego Scale (CBS). The same tests were performed after completion of the treatment protocol.

## C. Model Identification

For each subject, we took the recorded time series of the horizontal target location and hand position, expressed in degrees with respect to the body midline — one sample for each individual movement. Eqs. 3 - 4 define a non-linear discrete-time state-space dynamical model in which the quantity  $b(t)$  is the state variable. Model parameters ( $A_n$  and  $B_n$ ) were identified using a prediction error method. Parameter  $H$  was kept fixed and set to  $H = 90^\circ$ . All calculations were carried out with MATLAB’s System Identification Toolbox. We treated the data from different sessions as separate experiments, but assumed that the model parameters do not change in the course of the whole recovery process. In addition to model parameters, the identification procedure gives estimates of the time course of the internal state ( $b(t)$ ) during each session. As a measure of fitting performance, we calculated the correlation coefficient  $R$  between the observed and predicted performance. Its square,  $R^2$ , expressed in percent, can be interpreted as the fraction of variance accounted for (VAF) by the model.

## III. RESULTS

### A. Simulations

We first used the model to simulate a prism adaptation task. Simulations are based on reaching movements toward two targets, located at the extreme left and the extreme right of the visual space. The simulated prism produced a  $10^\circ$  shift toward either the right or the left. The experiment was repeated with a healthy subject (for which we assumed an initial value  $b(0) = 90^\circ$ ) and a neglect subject (for which we

TABLE I: Subjects data and model fitting. BIT: Behavioural Inattention Test; BI: Barthel Index; RT: Reading Test; CBS: Catherine Bergego Scale.  $A_n$ : retention rate;  $B_n$ : recovery rate; VAF: variance accounted for.

ID	Demographic data					Neuropsychological evaluation				Model fitting		
	sex	age	side	type	disease duration (weeks)	BIT (0-146)	BI (0-100)	RT (0-6)	CBS (0-30)	$A_n$	$B_n \times 10^{-5}$	VAF (%)
S1	F	88	R	ischemic	2	63	7	4	20	0.998	0.0003	89
S2	F	67	R	hemorrhagic	4	104	12	3	9	0.998	683	97
S3	M	52	R	hemorrhagic	3	63	19	4	19	0.998	924	96
S4	F	78	R	hemorrhagic	2	87	75	3	24	0.999	77.1	97

set an initial value  $b(0) = 80^\circ$ ). The simulation results are summarised in Figure 2. After application of the prism, in order to reach the target the subject must move in the opposite direction with respect to the deviation induced by the prism. Healthy subjects adapt gradually to the prism, with a similar trend with both prism types. In both cases, the reaching error gradually reduces as the subject learns to compensate for the perturbation. When the prism is removed, the subject continues to move in the opposite direction with respect to the perturbation (aftereffect), which gradually washes out. USN subjects are equally capable of adapting to both left and right prisms. However, the two prisms have very different effect on neglect. Adaptation to the right prism results in a gradual increase of  $b(t)$ . In contrast, adaptation to the left prism results in a small decrease, corresponding to a worsening of the neglect symptoms. These results are in agreement with the experimental findings: adaptation to a right prism improves the neglect symptoms [6], whereas adaptation to a left prism has no effect [21] or is even detrimental.

#### B. Model-based analysis of experimental results

The neglect recovery model was also used to interpret the temporal evolution of performance in a rehabilitation trial. Figure 3 summarizes, for a typical subject, the observed performance (black traces) and the model predictions (red traces). We also displayed, for the first and last training session, the relation between target location and final hand position and the corresponding neglect model according to Eq. 1. This plot suggests that the distortion in the target representation in the left hemisphere is gradually reduced as training proceeds. The subject exhibits some variability in movements, especially in the early sessions. The overall model fitting performance is summarised in Table I. The estimated parameter values suggest that different subjects have different recovery rates. This may reflect the between-subjects differences in size and location of the cortical lesions. In contrast, the retention rate likely reflects basic features of cortical plasticity. The retention rate values are highly uniform across subjects, corresponding to a time constant of  $\tau = -1/\log A_n = 500$  trials. The retention rate likely reflects basic features of cortical plasticity. This is about ten times the time constant estimated in adaptation experiments (visuomotor rotation and/or force fields) or in robot-assisted rehabilitation trials [12] and is consistent with the observation [6] that neglect recovery lasts much longer than the effect of prism adaptation. Notably, subject S1 exhibits a lower VAF

value than other subjects. This may be due to presence of other symptoms, which the model does not explicitly account for.

#### IV. DISCUSSION AND CONCLUSIONS

Different from approaches that explicitly focus on neural representations and the way they are affected by cortical lesions – e.g. [15], our proposed model is formulated in terms of general principles and observable quantities. As such the model not only makes qualitative predictions, but can be used to interpret the trial-by-trial evolution of the neglect symptoms in individual subjects.

##### A. The model reproduces empirical observations in prism adaptation experiments

One major compensatory effect of short-term prism exposure is a mismatch between motor commands and visual targets. After adaptation, straight-ahead finger movements are shifted in a direction opposite to the optical deviation, indicating that internal visual and motor representations have been realigned. Our computational framework predicts that right prism adaptation is beneficial to neglect [6]. In particular, we propose that neglect recovery is facilitated by the leftward ‘endogenous’ movements induced by adaptation. This is not the only possible explanation of the empirical observations; in fact, alternative models are possible. The proposed modelling framework could be used to compare alternative theories and to contrast them with empirical findings.

##### B. The model facilitates interpretation of rehabilitation training and may suggest optimal forms of treatment

One major feature of the model is that it can be used to interpret the performance time series and to detect implicit information in the performance time series of individual subjects. In fact, the application of a similar model to robot-assisted stroke rehabilitation trials has suggested that the estimated model parameters could be used, in individual subjects, to quantify the ongoing effect of treatment and to predict its outcome [12]. Furthermore, a parametric description of the dynamics of the recovery process could be directly used to derive customized treatment solutions that can maximize the recovery outcome[14].

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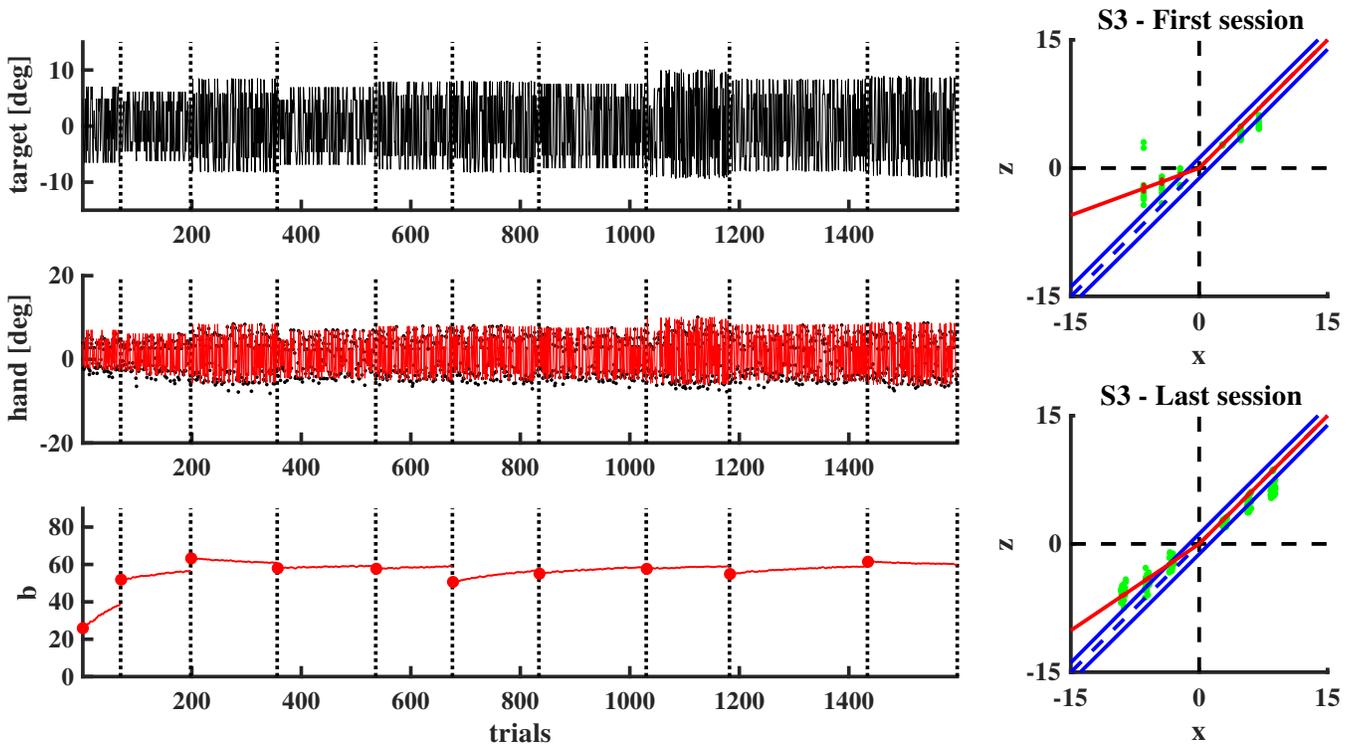


Fig. 3: Model fitting. Left, from top to bottom: target positions ( $y_T(t)$ ), hand movements ( $x(t) = z_T(t)$ ) and neglect ( $b(t)$ ). Right: Distorted internal representation of visual stimuli, on first and last training session. In all cases, black traces denote experimental data, red traces denote model predictions. Blue lines indicate the size of the visual targets, green dots indicate final hand positions in experimental data (one point per trial on that session). All measures are expressed in degrees.

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